III. REMARKS

United States Serial No. 10/520,239 was filed on July 18, 2005. The Office mailed a Restriction Requirement on February 1, 2007. Applicant elected to prosecute the claims 26-35 in the present application and traversed the restriction between claims 16-25 and 26-35. The Examiner has made the Restriction Requirement final and has withdrawn claims 16-25 from consideration. Applicants respectfully request reconsideration and allowance of claims 16-35.

Restriction Requirement

The Examiner required restriction under 35 U.S.C. §§121 and 372 to one of the following Groups:

Group I: Claims 16-25, drawn to a Ruthenium (II) compound of formula (I); and

Group II: Claims 26-35, drawn to a method of treating and/or preventing cancer by administering a therapeutically effective amount of a Ruthenium (II) compound of formula (I).

It was alleged that the claims of Groups I and II do not relate to a single inventive concept under PCT Rule 13.1. The Examiner has maintained his position and has made the Restriction Requirement Final. The basis of the finality of the Restriction Requirement is that the chemical structure of the Carmona reference allegedly anticipates the structure of pending claim 22.

Applicants respectfully continue to disagree with the Examiner's position regarding the Carmona reference. The ruthenium (II) compound of pending claim 22 is absolutely not anticipated by Carmona. As recited in claim 22, R_{1c} and R_{3c} of the ligand are independently phenyl or substituted phenyl. The Carmona

reference does not disclose or suggest this chemical structure. In the chemical structure of Carmona, R_{1c} and R_{3c} of the ligand must be **methyl**. Therefore, the entire basis for the restriction requirement is erroneous.

Example 4 of Section 10.24 of the PCT Search and Examination Guidelines (PCT/GL/ISPE/1, Page 81) is similar to the present situation:

10.24 - Example 4

Claim 1: Use of a family of compounds X as insecticides.

Claim 2: Compound X_1 belonging to the family X.

The PCT Search and Examination Guidelines clearly state that there is unity of invention between the subject matter of claims 1 and 2, provided that X_1 of claim 2 possesses insecticidal activity and the special technical feature in claim 1 is the insecticidal use.

In the present application, the claims of Group I are directed to certain ruthenium (II) compounds. The claimed ruthenium (II) compounds possess anticancer activity. The claims of Group II are directed to a method for treating cancer by administering a therapeutically effective amount of a ruthenium (II) compound to a subject in need of treatment.

Applicants respectfully submit that the present application is quite similar to Example 4 of the PCT Search and Examination Guidelines where unity of invention was upheld. The ruthenium (II) compounds of claims 16-25 possess anticancer activity and claims 26-35 are drawn the use of ruthenium (II) compounds in a method for treating and/or preventing cancer. Again, the Carmona reference does not anticipate the compound of claims 16, 22 and 26.

For the reasons set forth hereinabove, Applicants respectfully request reconsideration of the restriction requirement and submit that it is not proper in the present application. The restriction requirement should be withdrawn and the claims of Groups I and II be rejoined for prosecution in the present application.

35 U.S.C. §112

First Paragraph

It is alleged that claim 26 is only enabled for the treatment of ovarian adenocarcinoma with some of the claimed compounds. Applicants respectfully traverse this rejection. To begin, the Specification includes working examples of successful *in vitro* testing of exemplary ruthenium (II) compounds. Applicants disagree with the Examiner's position that Example No. 2 shows "no apparent activity." The Specification at Page 26 shows the results for the *in vitro* testing of exemplary ruthenium (II) compounds. Preceding the table of results, the Specification discloses that the ruthenium (II) compounds have an IC50 of less than 150 um, preferably less than 100 um, and more preferably less than 50 um. Examples Nos. 1 and 3-6 all fall within the disclosed most preferable range. The results for Example No. 2 fall within the range of "less than 150 um" disclosed in the Specification. According to the Federal Food and Drug Administration, the IC50 value represents the concentration of a drug that is required for 50% inhibition *in vitro*. Therefore, the ruthenium (II) compound of Example No. 2 does indeed possess anti-cancer activity as it falls within the broadest disclosed range of less than 150um. It simply takes a larger dose of the ruthenium (II) compound of Example No. 2 as compared with the compounds of Example Nos. 1 and 3-6.

Additionally, most cancer researchers hold either a Ph.D., M.D., or a combined M.D./Ph.D. degree and possess years of clinical training in oncology and/or basic science research training. Therefore, there is a high level of skill in the relevant art. Additionally, the Specification provides ample guidance and

support with respect to the chemical structures of the ruthenium (II) compounds, methods of synthesis of the ruthenium (II) compounds, and protocols of testing the compounds.

The Specification expressly discloses that the claimed ruthenium (II) compounds may be used to treat tumours of all forms of neoplastic growth including tumours of the lung, liver, blood cells, skin, pancreas, stomach, colon, prostate, uterus, breast, lymph glands, bladder and ovary. See Specification at Page 18, Lines 10-13. The disclosure of the use of the compounds to treat the above-identified cancers, when taken in light of the test results relating to the ovarian cancer cell line, provide enablement for the full scope of claim 26. With respect to the alleged "limited examples" provided in the Specification, it has been held that claims are not invalidated simply because specification embodiments do not contain examples explicitly covering the full scope of the claim language." *LizardTech, Inc. v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, (Fed. Cir. 2005). Accordingly, Applicants respectfully submit that the claims are fully enabled for treating "cancer" and should not be limited only to treatment of ovarian cancer.

It is also alleged that claim 26 is only enabled for compounds of a select ligand of formula (I) and does not provide enablement for using all claimed ligand types of formula (I). Applicants respectfully traverse. The specification clearly describes that Y and Y' may be selected from O, S or NR^{16}. See Specification at Page 4, Lines 10-12.

Broad generic claims relating to methods for preparing bacterial strains that produce certain amino acids were held to be properly enabled by the deposit of just four bacterial strains capable of producing amino acids. *Ajinomoto v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 56 USPQ2d 1332 (Fed. Cir. 2000). In *Ajinomoto*, the claims were directed to a method for mutating bacteria to overproduce a select amino acid. The method involved the use of mutated donor and recipient bacterial strains. The bacterial strain was mutated to destroy the

regulatory and metabolic pathways of the strain. Therefore, the strain would overproduce the selected amino acid without metabolizing it. The independent claim recited was not limitated as to the identity of the donor or recipient bacterial strains and therefore covered <u>any and all</u> bacteria strains which would overproduce amino acids. The written specification described only four bacterial strains for use in the claimed invention. Nevertheless, the Federal Circuit held that the disclosure of only four strains of bacteria enabled the full scope of the generic claims. The Federal Circuit reached its holding even though there were innumerable bacterial strains covered by the generic claims that were not disclosed in the specification or deposited.

Furthermore, "[T]he test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). In the present application, Applicants have specifically exemplified seven ruthenium (II) compounds for use in the claimed method of treating cancer. The detailed of the synthesis of these compounds is disclosed in the Specification at Pages 21-24. The protocol and results for testing the exemplified ruthenium (II) compounds can be found in the Specification at Pages 24-26. Consequently, there is considerable direction and guidance set forth in the Specification as to the structure, synthesis and testing of the ruthenium (II) compounds to enable one having ordinary skill in the art to make and practice the claimed invention. Most, if not all, researchers of cancer hold either Ph.D., M.D. or combined M.D./Ph.D. degrees and possess years of clinical oncology training and/or basic science research training. None of the experimentation to synthesize and test other of the ruthenium (II) compounds would be undue given the guidance provide by the Specification and the high level of skill in the art. In view of the fact that the Specification discloses and specifically exemplifies seven different ruthenium (II) compounds, Applicants respectfully submit that the Specification is enabled for using the full scope of the ligand types of formula (I).

Additionally, MPEP §2164.02 specifically states that "[F]or a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of the level of skill, state of the art, and the information in the specification) would expect the claimed genus could be used in the manner without undue experimentation." As set forth above, the level of skill in the art is very high, protocols for testing the efficacy of potential anti-cancer drugs is well known and the is ample guidance in the Specification regarding the structure, synthesis and testing of the claimed ruthenium (II) compounds. Therefore, the specifically exemplified embodiments of the ruthenium (II) compounds provide enablement for the full scope of the generic claims.

The issues of utility and enablement are closely related. Utility for a genus was found to be supported through a showing of utility for <u>one species</u>. *In re Gardner*, 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). In the particular case, the Specification discloses and exemplifies the anti-cancer efficacy of more than one species of the ruthenium (II) compounds. Accordingly, Applicants respectfully request that this rejection be withdrawn.

It is alleged that claim 26 does not reasonably provide enablement for preventing cancer. In the spirit of compact prosecution and without conceding that the claim is not enabled for preventing cancer, claim 26 has been amended by deleting the language "and/or preventing". It is submitted that this rejection is now moot. Applicants also submit for the record that inhibition of cancer metastasis is encompassed by the term "treating".

<u>Second Paragraph</u>

Claims 26-35 have been rejected under 35 U.S.C. 112, second paragraph, for the reasons stated in Paragraphs 7-11 of the Office Action.

With respect to Paragraph 7 of the Office Action, it is alleged that the use of the term "subject" renders claim 26 indefinite. Claim 26 has been amended as suggested by the Examiner to include the language "subject in need of treatment." Therefore, this rejection is moot and should be withdrawn.

With respect to Paragraph 8, it is alleged that a countering cation is not possible and therefore m = -1 can never exist. Applicants respectfully traverse. X may be neutral or bear a negative charge. The indefinite article "a" has been construed by the Federal Circuit to mean one or more than one. Thus, in this case, the use of the indefinite article "a" should be construed to one having ordinary skill in the art to refer to a single or a double negative charge. Y-L-Y' is not limited to a single negative charge; it may bear a double negative charge. When X carries a negative charge and Y-L-Y' carries a double negative charge, m will be -1. Therefore, the presence of a counterion, ie, a countering cation, would be required.

With respect to Paragraph 9, it is alleged that Y-L-Y' of formulae (II) to (IX) are construed to carry a double negative charge, for which there is no antecedent basis. Applicants disagree. The Federal Circuit has "repeatedly emphasized that an indefinite article 'a' or 'an' in patent parlance carries the meaning of 'one or more' in open-ended claims containing the transitional phrase 'comprising.'" *KCJ Corp. v. Kinetic Concepts, Inc.*, 223 F.3d 1251, 1356 (Fed.Cir. 2000). *See also Crystal Semiconductor Corp.*, 246 F.3d at 1347. Independent claim 26 recites that ligand Y-L-Y' bears "a" negative charge. The article "a" has been construed by the Federal Circuit to mean one or more than one. Thus, in this case, the use of the article "a" should be construed to one having ordinary skill in the art to refer to a single or a double negative charge. Furthermore, the specification teaches, "[T]he ligand may bear a single negative charge or may have more than one negative charge, eg, by being a dianion." See Specification at Page 9 at Lines 21-23. Therefore, Applicants respectfully submit that claim 30 possesses proper antecedent basis. There is no need for charge delocalization between the T and T' atoms, as long the requirement of the claim

for a portion of the negative charge on the ligand is bourne by both Y and Y', which will be the case if the ligand is a dianion, i.e. there is negative charge on both Y and Y'.

With respect to Paragraph 10, it is alleged that there is insufficient antecedent basis for formula (XIII) because the ligand is incapable of charge delocalization between T and T' or T" and T'". As stated above, there is no need for charge delocalization between the T and T' atoms, as long the requirement of the claim for a portion of the negative charge on the ligand is bourne by both Y and Y', which will be the case if the ligand is a dianion, i.e. there is negative charge on both Y and Y'. Therefore, Applicants respectfully submit that claim 31 possesses proper antecedent basis.

With respect to Paragraph 11, it is alleged that the scope of the claims in not understood. It is specifically alleged that the absence of a position charge location in formula (I) renders the claim indefinite. Applicants respectfully traverse this rejection and submit that formula (I), when read in light of the balance of the claim and the Specification, is clear to one having ordinary skill in the art. The Specification and claim 26 states that the ligand Y-L-Y' carries a negative charge. If the ligand is taken in isolation this will be the case. However, when the ligand complexes the Ru(II) atom a covalent bond is formed with the electrons that provide the negative charge. The representation given in the Specification is conventional in the art, see, for example, Kramer where in compound 4 a chloro ligand is present. This ligand in isolation would be represented as Cl^-. Therefore, Applicants respectfully request that this rejection be withdrawn.

Should there be any questions regarding the above amendments or remarks, the undersigned attorney would welcome a telephone call.

Respectfully submitted,

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